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AUTHOR(S):

Watanabe, Yutaka

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STUDIES ON THE VISCEROGENIC REFLEXES.

From the 2nd Surgical Divison, Kyoto University Medical School

(Director: Prof. Dr. YASUMASA AOYAGI)

by

YUTAKA WATANABE.

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INTRODUCTION :

For experimental studies of sensory nervous pathways in animals, we need objective, observable and constant indicators. Therefore, I used as indicators the visceromotor reflex, vomiting reflex, vasomotor responses, inhibitory reflex of intestinal movement and change of respiration. Recently, CHUJI KIMURA and KAZUMASA OHBA have discovered a method causing visceral pain in human beings: injection of vagostigmin (eserin) acethylcholin (ACH) solution into the wall of the alimentary canal. So, as stimulus to a viscus, I used this ACH-method as well as other stimuli, such as electric faradization or traction of the mesentery.

1. CHANGES OF RESPIRATION.

The type of respiration may be changed by visceral Pain. The changes of respiration were recorded on a kymogramm directly or indirectly.

The stimuli used were : (1) electric faradization, (2) traction of the mesentery, (3) dropping of ACH solution (0.1gm. 20cc) 0.05-0.1cc on the wall of the intestine, or injection of it into the wall of the intestine.

The results of experiments :

6-12 seconds after ACH solution was dropped on a point of the intestinal wall or rabbits, the site became spastic, and the curve of respiration showed apnea, superficial or deep respiration, or hyperpnea. Other stimuli caused almost the same changes of respiration. (Fig. 1.)

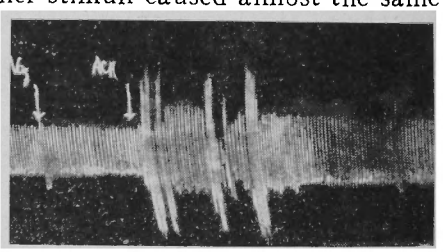


Fig. 1. Respiration curve. ACH (0.1 Gram/20cc) 0.05cc dropped on the ileum of rabbit.

The results of the experiments on respiratory reflexes after sectioning various nerve trunks are shown in table 1, 2 and 3. From my experiments of vagotomy and transection of the spinal cord at the level of the thoracic segments, or of vagotomy and posterior rhizotomy, we can assume that some of the afferent fibers from the ileum of cats or rabbits pass through the vagi and others through the splanchnic nerves entering in the posterior roots at Th3-L3, mostly Th6-3.

Table I. Respiratory Change following Visceral Stimulation after various Denervation.

Stimulated Site	Stomach			Ileum			Appendix			Colon		
Reaction	+	−	÷	+	−	÷	+	−	÷	+	−	÷
Nerve intact	17			11			4			2		
Vagotomy	1			3			1					
Splanchnectomy		12		7	1	1	5			1		
Vagotomy-splanchnectomy	3	1		4	5		1	2				
Splanchnectomy-exstirpation of ganglion solare	1	3		4	7			2			1	
Splanchnectomy-lumbar sympathectomy					2	1	1					
Splanchnectomy-lumbar sympathectomy-vagotomy	3		1		2			2				
Transection of upper thoracic cord			1	6	1	1		1	1	1		
Transection of upper thoracic cord-splanchnectomy			1	1	1			1			1	
Transection of upper thoracic cord-splanchnectomy-vagotomy					1							
Transection of lower thoracic cord				5								
Transection of lower thoracic cord-vagotomy				1			1					
Transection of lower thoracic cord-vagotomy-splanchnectomy					2							
Posterior root section (Th4 …… Th13)	3	3		5	1		3	1				
(Th4 …… L3)		1			1							
Subarachnoid alcohol injection	2	1	1			2	1	3				
Subarachnoid alcohol injection-vagotomy		2		1	1		1	1			1	
After 10% TEAB injection (0.3–2.0 cc)	5			12						2	1	

Numbers are cases. + : Respiratory change was perceived.
− : No respiratory change.
÷ : Undetermined.

Table 2. Respiratory Change following Visceral Stimulation after Vagotomy and Transection of the Thoracic Spinal Cord.

Case	Level of Transection of the Thoracic Spinal Cord	Stimulated Site		
		Stomach	Ileum	Appendix
(1) 2.8Kg Cat	Th 4		−	
(2) 1.9Kg Cat	Th 5	−	−	−
(3) 1.9Kg Cat	Th 5 … 6	−	−	−
(4) 4.0Kg Cat	Th 5	−	−	
(5) 1.3Kg Cat	Th 7		−	
(6) 1.8Kg Cat	Th 6	−	−	−
(7) 3.5Kg Cat	Th 6	÷		−
(8) 3.5Kg Cat	Th 4	−	−	−
(9) 1.5Kg Rabbit	Th 3	−	−	−
(10) 1.6Kg Rabbit	Th 8 … 7	÷	÷	
(11) 1.6Kg Rabbit	Th 4 … 5	−	−	
(12) 1.7Kg Rabbit	Th 3	−	−	
(13) 2.2Kg Rabbit	Th 8		+	
(14) 2.2Kg Rabbit	Th 5 … 6		−	
(15) 2.2Kg Rabbit	Th 5 … 6		−	

Tabl 3. Respiratory Change following Visceral Stimulation after Posterior Rhizotomy and Vagotomy.

Upper limit of level of disappearance of respiratory change		Stimulated Site		
		Stomach	Ileum	Appendix
(1) 2.6Kg cat	Th 5 … Th 13 (Below this crushed)	÷	—	—
(2) 2.6Kg cat	Th 3 … Th 13 〃	—	—	—
(3) 4.0Kg cat	Th 4 … Th 13 〃	÷	—	
(4) 1.2Kg cat	Th 6 … Th 12 〃		—	—
(5) 1.8Kg rabbit	Th 4 … Th 11 〃	÷	÷	
(6) 2.9Kg cat	Th 5 … Th 13 〃	—	÷	
(7) 2.9Kg cat	Th 5 … Th 13 〃	÷		
(8) 4.0Kg cat	Th 3 … Th 13 〃	÷	÷	
(9) 4.0Kg cat	Th 3 … L 3 〃	—	—	

2. PUPILLO-DILATOR REFLEX

Using the same stimulus as above mentioned, I also investigated the pupillo-dilator reflex (BAIN and others) in cats to study afferent nervous pathways from the alimentary canal.

The results are almost the same as those of section 1. Afferent nerves pass through four nerve trunks :

(1) Sympathetic nerves → Splanchnic nerves → Posterior roots → Spinal cord. For instance in the duodenum, afferent fibers reach the spinal cord from Th3 to L1, and in the ileum from Th5 to L1.

(2) Sympathetic ganglia → communicating branches → posterior roots → Spinal cord.

(3) Both vagi.

(4) Phrenic nerves, when the central portion of the diaphragmatic peritoneum is stimulated.

3. INTESTINAL INHIBITORY REFLEX

The motility of the intestine was studied in patients who had fecal fistula. A baloon was inserted into the ileum or the colon 15 50cm. distal to the orifice of the fecal fistula, and motility of the intestine was recorded on the kymogram.

ACH was injected in the submucous tissue around the orifice of the fecal fistula. The kymogram showed the inhibition of motility and decreased tonus, when the patients felt cardialgia. (Fig. 2.)

Therefore, I used this inhibition reflex as an indicator of visceral noci reflex in animals.

Material and methods : Cats and rabbits were used. The methods were all the same as stated above.

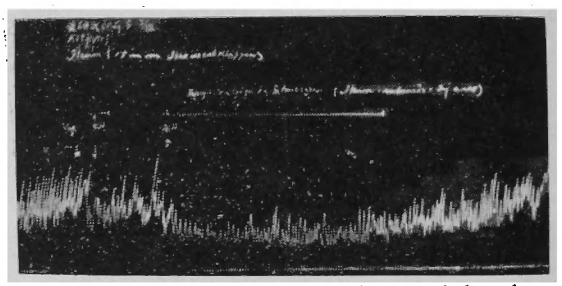


Fig. 2. Effect of VAG (eserin)ACH, injected into the wall of fecal fistula of a man, aged 50 male, on the motility of the ileum at a point 15 cm proximal to the fistula. He has complained of abdominalpain, lasted 10 minutes.

Results :

(1) when 0.05-0.1 cc of ACH (0.1gm./20cc) was dropped on the wall of the ileum, appendix or colon, the tonus of the stomach and the duodenum decreased and their motility was inhibited. The same phenomena were demonstrated in other distant parts of the alimentary canal: (Fig. 3.)

(2) The phenomena of the inhibitory reflex following various denervations are shown in table 4. Adrenalectomy did not have much influence on this reflex.

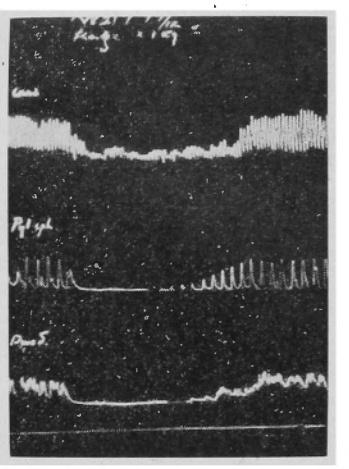


Fig. 3. The motility of cardia, pylorus and duodenum of a cat (2.1Kg F) after injection of ACH (0.1/20 0.05cc in the ileum. Note the inhibiton of motility of each tract.

Discussion ;

The results of my experiments proved that adequate stimulation of the alimentary canal caused the inhibitory reflex with abdominal pain. The afferent impulses from the ileum are conducted through sympathetic nerves → splanchnic nerves → dorsal roots to spinal cord, and through vagal nerves, too.

Since in my experiments motility of the alimentary canal was recorded at a distant area from the stimulated point, we can exclude

Table 4. Intestinal Inhibitory Reflex following Visceral Stimulation after Denervation.

Denervation	Motility / Stimulat. Site	Stomach +	Stomach −	Stomach ÷	Intestine +	Intestine −	Intestine ÷	Colon +	Colon −	Colon ÷
Nerve intact	Small intestine	12	1		6	3	2	7	1	
	Large intestine	3						3		
	Stomach	2	4		2					
	Appendix	4	1		3			1		
	ACH intramuscular			2		1	1			
Splanchnectomy	Small intestine	2	1	2				1		
	Colon	1								
Splanchnectomy-adrenectomy	Ileum	3	1							
Exstirpation of ganglion solare	Ileum	1	3							
Splanchnectomy-lumbar sympathectomy	Ileum		4							
Splanchnectomy-vagotomy	Ileum		3							
Vagotomy	Ileum	4								
	Colon	1								
Posterior rhizotomy Th4···Th12	Ileum	3	2	4						
Th3···L3	Ileum		2							
Transection of upper thoracic spinal cord	Ileum		3	4						
Transection of upper thoracic spinal cord and vagotomy	Ileum	1	1							
Transection of Th 12	Ileum	2								
Removal of spinal cord (Th 5 ··· L 1)	Ileum	4	1	1		1				
	Appendix			1						1
Subarachnoid alcohol injection	Ileum		4			4				
	Appendix					1	1			
After intravenous injection of 10% TEAB		2	1							

+ ; Intestinal inhibitory reflex was positive. − ; It was negative. ÷ ; Undetermined.

myenteric reflex.

4. SUPPLEMENTARY STUDY ON THE VOMITING.

Nausea and vomiting are digestive symptoms and considered as a noci-reflex against noci-stimuli. My study on vomiting was restricted to the reaction caused *by stimulating* an abdominal viscus and to the afferent nerves conducting emetic impulses. I used the ACH-method as a chemical stimulus to vomiting, and faradization as a contrast method.

A. Experiments on a decerebrate cat.

The above mentioned stimuli were applied to the alimentary canal of a cat decerebrated by SHERRINGTON'S method. When the ACH-method was used, contrast experiments were performed every time, such as faradization or pulling up the mesentery. When 0.5cc of ACH (0.1gm /4cc) was injected into the intestinal wall after manipulation or fardization of the mesentery, vomiting was induced. Faradization of the mesentery, biliary tracts or splenic hilum after subcutaneous injection of 0.05% vagostigmin or ACH (0.1gm./4cc), or after distension of the stomach with water, caused vomiting usually with latent time of 1-3 minutes.

But after faradization of the parietal peritoneum, the diaphragmatic peritoneum or other somatic nerves, vomiting did not occur.

Therefore, vomiting should be cosidered as a viscerogenic or vagus symptom, but not a peritoneal or somatic symptom.

2) After section of the vagi, vomiting did not occur following faradization. However, about 30 minutes after subcutaneous injection of vagostigmin or 0.2cc of ACH solution (0.1gm/4cc) the decerebrate or vagotomized cat vomited within a minute after electric stimulation of the mesentery.

Subcutaneous injection of the some amount of vagostigmin or ACH solution alone could not cause vomiting. These results indicate that the action of ACH or of vagostigmin on the afferent vagal nerve endings facilitate vomiting and that the sympathetic trunk is also a path of the emetic impulses.

3) Denervation experiments on cats.

a. Vagotomy and splanchnectomy.

b. Phrenicotomy and transection of the spinal cord at the level of the 2nd, 3rd and 5th thoracic vertebrae.

c. Vagotomy and phrenicotomy.

d. Vagotomy, phrenicotomy and splanchnectomy.

e. Vagotomy, phrenicotomy and extirpation of the ganglion solare.

In none of these experiments vomiting could be induced by any method.

In the cases in which the spinal cord was removed below the level of the 2nd, 3rd or5th thoracic vertebrae, vomiting could be induced only by electrical stimulation of the gastric vagus. Therefore, vagal and sympathetic nerves conduct the afferent emetic impulses, but vagi play the primary role.

B. Experiments on vomiting caused by stimulation of the duodenum of unanesthetized cats.

HERRIN and MEEK reported that continuous distension of intestinal fistulae in dogs caused anorexia and vomiting. SHRAGER and IVY found that the distension of the gall bladder and biliary duct in dogs caused nausea, vomiting and distress. With unanesthetized cats, I tried an experiment to cause vomiting by stimulation of the duodenal mucous membrane. First I made a duodenal fistula in a cat and then injected slowly or rapidly N/5-10 HCl 3-5-10cc, ACH(0.1gm/20cc) 3-10cc or water into the duodenum through a catheter inserted in the duodenal fistula. During the experiment, the cat was quiet. Within several minutes the cat vomited. (Fig. 4)

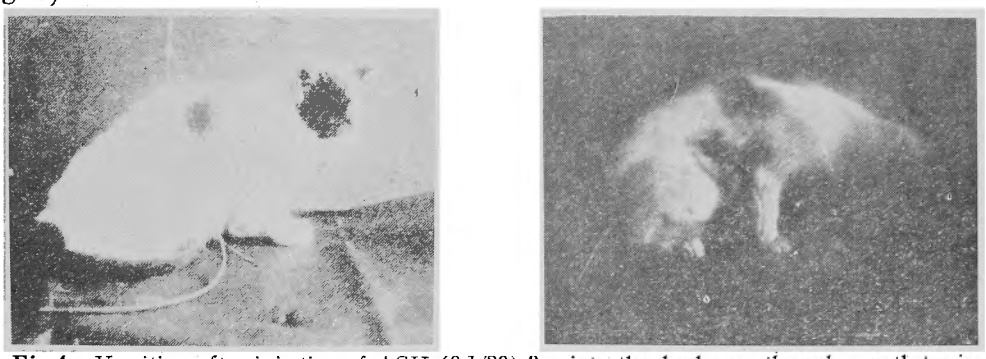


Fig 4. Vomiting after injection of ACH (0.1/20) 3cc into the duodenum through a catheter in the duodenal fistula.

Injection of HCl or ACH into the duodenum causcd inhibition of motility of the proximal part of the duodenum and of the stomach as in fig. 5. When given by mouth, these chemicals did not induce vomiting.

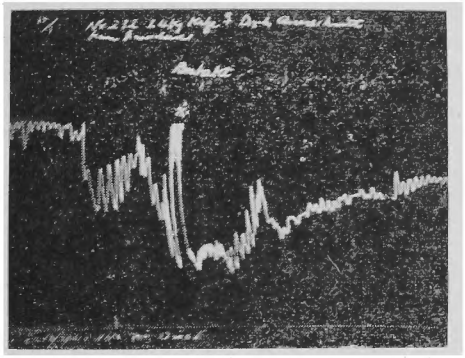
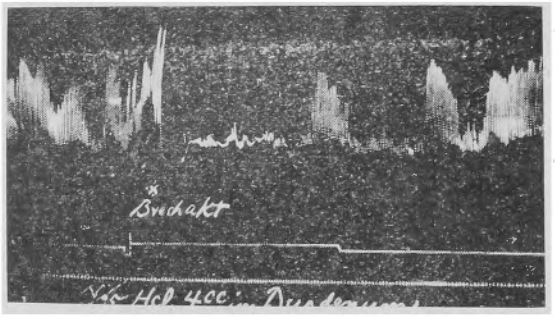


Fig. 5. The motility of stomach of cat (1.4 Kg, F) by vomiting after injection of N/5 HCl 10cc into the duodenum through fistula.
* vomiting



The motility of proximal duodenum after injection of N/5 HCl 4cc into the distal duodenum.
* vomiting

After vagotomy, the cat did not vomit, but after subcutaneous injection of vagostigmin-ACH, it vomited after the same stimulus. Bilateral abdominal sympathectomy and splanchnectomy inhibited vomiting completely. Inflammation of the peritoneum facilitated vomiting.

After phrenicotomy, the cat vomited by the same stimulus, but not after tran-

section of the spinal cord (T4, T5, T6). From these experiments it is clear that the afferent nervous pathways of vomiting are vagal and sympathetic nerves.

C. Vomiting and adrenergic and cholinergic changes in blood.

One may wonder whether the vomiting caused by ACH in my experiments is neurogenic or humoral, because ACH may induce vomiting by stimulation of the medullary vomiting center through the general circulation. ACH injected sudcutaneously can cause vomiting. Therefore I investigated adrenergic and cholinergic changes in blood by MUSSER-GRIM'S method when the duodenm was stimulated by ACH, faradization or putting HCL solution into it.

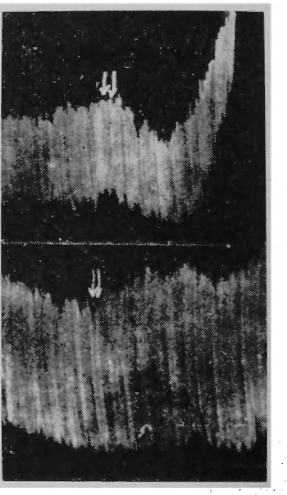


Fig. 6. Upper : Effect of blood 1cc of the cat after injection of ACH in the wall of the ilem,or the motility of isolated duodenal loop of rabbit.(No. 11 on Table 3) (This is Musser-Grimm's methodm) Lower : Before injection.

Before stimulation, the blood of decerebrate cats showed sometimes adrenergic and sometimes cholinergic reactions. For about 5minutes after

Tabl 5. Changes of the Humoral substances in Blood following Visceral Stimulation, particulary at vomiting.

Cases	Humoral Substances in Blood	
	Before	After administration of ACH-solution
(1) 1.7Kg cat	N	Adr. in 2 min. after vomiting (ACH injected in duodenum) Chol. in 15 min.
(2) 3 Kg cat	N	Adr. in 5 min. after nausea (ACH injected in duodenal-wall.)
(3) 1.2Kg cat	N	N. soon after vomiting (by faradization).
(4) 2.0Kg cat	N	Adr. in 1 min. after vomiting (ACH 0.1/3 cc solution 0.1 cc injected in the wall of ileum.
(5) 5 Kg dog	N	Adr. in 2 min. after injection of ACH-solution in ileumwall. Adr. in 40 min. N. in 60 min. (No vomiting)
(6) 1.6Kg cat	N	Chol. in 5 min. after injection of ACH in duodenum. N. in 40 min.
(7) 1.4Kg cat	Chol.	Adr. in 2 min. after vomiting.
(8) 1.7Kg cat	N	Adr. after injection of ACH (0.1/20cc) 10cc in duodenum. No vomiting.
(9) 3.0Kg cat	Adr. slight	Adr. in 1.5 min. after vomiting (by injection of ACH-solution (0.1/5cc) 0.1 cc into duodenal-wall. Adr. in 15 min.
(10) 2.3Kg cat	Chol. slight	N. soon after injection of ACH-solution to duodenal-wall. Adr. 30 min. after vomiting.
(11) 2.8Kg cat	Chol.	Adr. in 3 min. after injection of ACH-solution (0.1/5cc) 0.1cc to the duodenal wall.
(12) 2.5Kg cat	N	N. in 15 min. after injection of ACH in urinary bladder. No vomiting.
(13) 1.8Kg cat	Adr.	N. in 5 min. after injection of ACH-solutinn (0.1/5 cc) 0.2 cc in duodenal wall. Adr. in 2 min. after vomiting.
(14) 2.6Kg cat	Chol. slight	Adr. markedly in 18 seconds before vomiting. Adr. slightly. vomiting several minutes later.

Adr.……Blood showed adrenergic. Chol.……Cholinergic. N.……Not changed.

stimulation of the duodenum by ACH, the blood tended to be adrenergic and 30 minutes after stimulation completely cholinergic. (Table 5. Fig. 6.)

If vomiting is due to ACH in the blood, the blood, sould be cholinergic immediately after administration of ACH. Therefore, vomiting in my experiments must be a reflex phenomenon.

5. VASOMOTOR RESPONSE TO ACH METHOD.

A cat was anesthetized with 20% urethan 3-5cc and I measured the blood pressure through a carotid artery.

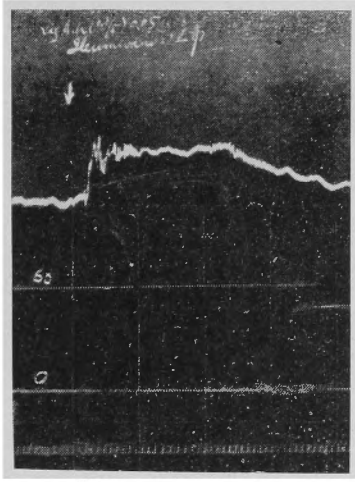


Fig. 7. When VAG-ACH (0.1/5) 0.05cc was dropped on the ileum of cat, blood pressure increased.

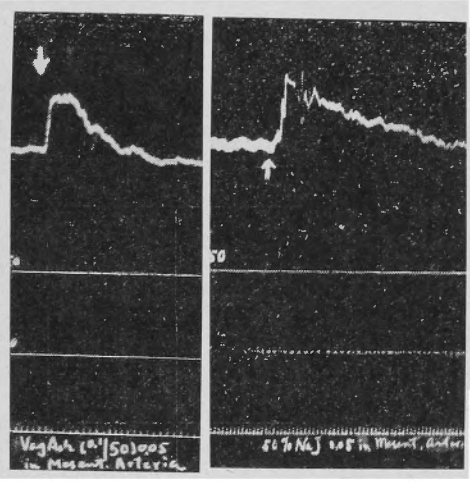


Fig. 8. Change of blood pressure when VAG-ACH (0.1/50) 0.05cc (leftside) and 50% NaI 0.05cc (right side) were injected in the superior mesenteric artery.

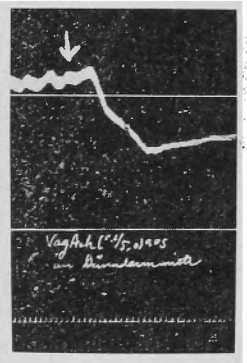


Fig. 9. Temporary increase of blood pressure, followed by decrease, when VAG-ACH (0.1/5) 0.05cc was injected in the wall of the intestine of a cat.

(1) When vagostigmin-ACH (0.1gm/5cc) 0.05cc was dropped on the cat's intestine, the blood pressure increased immediately and then grandually decreased. (Fig. 7.)

(2) When ACH 0.1gm/100cc 0.05cc or 50% NaI solution was injected into the mesenteric artery, the blood pressure increased markedly with contraction of the regional intestine. and then decreased. (Fig. 8.)

(3) When ACH was injected into the wall of the intestine,the blood pressure increased temporarily, and rapidly decreased. (Fig. 9.)

(4) When ACH was injected into the mesenteric vein, the blood pressure fell immediately down to 50-100mg Hg. It was the same as intramuscular injection of ACH (Fig. 10.) on the abdominal wall.

(5) Electric stimulation of the mesentery or the parietal peritoneum, increased the blood pressure in

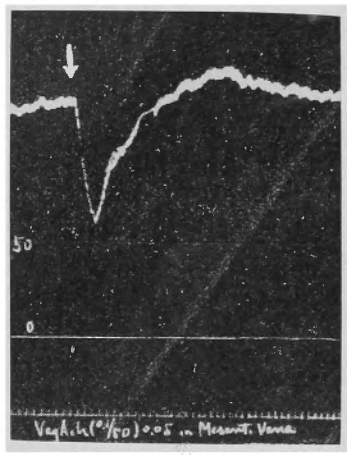


Fig. 10. Marked decrease of blood pressure of a cat, when VAG-ACH (0.1/50) 0.05cc was injected in the superior mesenteric vena.

general.

(6) After section of the sympathetic and splanchnic nerves, or after splanchnic anesthesia, this vaso-pressor reaction was abolished.

This reaction was also abolished by TEAB. Following transection of the spinal cord (T2, T3, T4, T5, T6), this reaction was diminished. Section of the vagi had no influence on this reaction.

6. COMPLEMENTAL STUDY ON TETRAETHYL AMMONIUM BROMIDE.

ACHSON and MOE found that TEAB blocked the conduction of impulses in the ganglia of the autonomic nerves. But in my studies of various reflexes, the afferent impulses were not blocked by TEAB.

TEAB is effective in decreasing abdominal pain in patients. Therefore, I tried to investigate the effect of TEAB on the motility of the alimentary canal. The results are shown in table 6.

Tabl 6. Effect of Tetraethyl Ammonium Bromide on the Motility of Alimentary canal.

Motility of Effect \ Dosis		mg/Kg 0.05	0.1	1.0	5	10	20
Stomach	Excitatory			5	8	3	1
	No change	1	6	3	1		
	Inhibitory		2	12	21	10	2
Small intestine	Excitatory	1	2	8	25	11	3
	No change	1	5	4	2	2	
	Inhibitory		2	8	5	4	
Colon	Excitatory	1	4	6	14	5	3
	No change		4	6	5		
	Inhibitory			3	9	3	

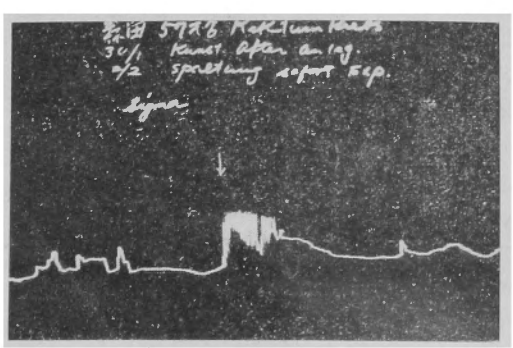
Number shows cases.

When the stomach is hypertonic and hyperkinetic, the motility of the stomach is inhibited by TEAB, and vice versa. This was true of our clinical cases.

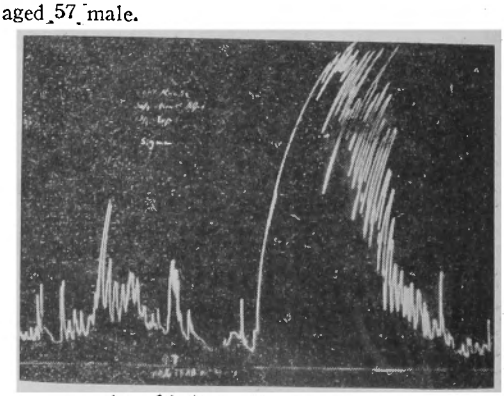
A 57 year old male was operated for carcinoma of the rectum. 2 days after the operation of making a colostomy, the motility of the sigmoid was not restored. Intravenous injection of 10% TEAB 1.0cc had an effect on the movement of the sigmoid.

After 2 weeks, motility of the sigmoid was restored. Inhibition of the motility of the sigmoid following injection of TEAB lasted for 3 minutes and

Fig. 11. The effect of intravenous injection of 10% TEAB 1--0.8cc on the motility of the sigmoid colon of a patient with carcinoma recti, aged 57 male.



a) ; 2 days after laparotomy.



b) ; 14 days after laparotomy.

was followed by marked increase of motility and tonus.

40 days after the operation, the motility of the colon became normal, and after the same dose of TEAB only the inhibitory effect was observed. (Fig. 11)

The same facts were observed in the small intestines of some patients with fecal fistula of the ileum.

In a cat with a fecal fistula of the ileum, I observed that 4 days after the operation, injection of TEAB 1.0cc made the small intestine hyperkinetic and hypertonic. But after motility of the intestine of the cat became hyperkinetic by subcutaneous injection of 0.05% vagostigmin 0.2cc, the same amount of TEAB made the intestine hypokinetic and hypotonic.

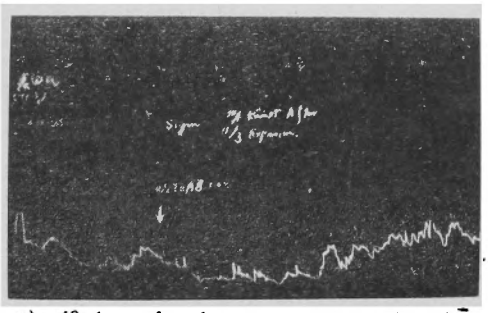
When adrenalin (1/1000) 0.5cc was injected intravenously in a cat the intestine became hypokinetic and injection of TEAB made it hypertonic. (Fig. 12)

These facts can be explained by the hypothesis that TEAB inhibits predominant side of sympathetic and parasympathetic tonus. TEAB works sometimes sympathicomimetically on motility and tonus of the alimentary canal, but its inhibitory effect is more marked.

7. VISCEROMOTOR REFLEX.

The theory of visceromotor reflex was described by MACKENZIE, whose interpretation was based on SHERRINGTON'S experiments, that abdominal rigidity occuring in visceral diseases is of reflex origin.

MILLER has shown that in the visceromotor reflex, the hindlimb muscles



c) ; 40 days after laparotomy. Note that the effect of TEAB varied according to the tonus of the colon.

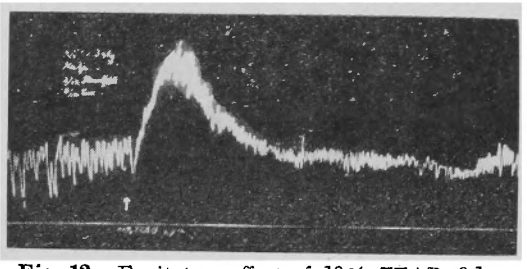
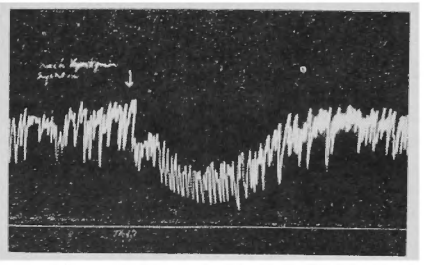
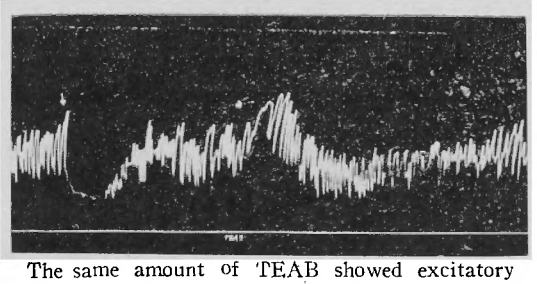


Fig. 12. Excitatory effect of 10% TEAB 0.1cc on the motility of intestine of a cat(2Kg) 4 days after laparotomy.



After subcutaneous injection of VAGOSTIGMIN, the intestinal motility became more active. At that time, the same amount of TEAB showed the inhibitory effect on it.



The same amount of TEAB showed excitatory effect on it, after intravenous injection of ADRENALINE (1/1000) 0.1cc.

as well as the abdominal muscles acted as effectors.

Method :

Decerebrate cats were employed (SHERRINGTON'S method). The contraction of the abdominal rectus muscle was shown by diagram by MILLER'S method. I used various stimuli for viscus, such as vagostigmin-ACH solution (0.1gm/5cc), other chemicals, faradization and pulling the mesentery with the fingers.

Results :

1) Faradization of the abdominal rectus muscles, which was followed by clonic contraction which gradually declined.

2) Stretching of the intestinal tract and traction of the mesentery caused reflex contraction of the abdominal muscles. Stronger reflex response was caused by faradization or mechanical stimulation of biliary tracts or hilum of the spleen.

3) Injection of vagostigmin-ACH (0.1 gm/5cc) in the intestinal wall caused clonic contraction of the abdominal muscles, which gradually rose to the maximum and declined slowly.

Subcutaneous or intramuscular injection of this chemical did not cause reflex contraction of the abdominal muscles. Injection of more dilute ACH solution (0.1gm/50cc-100cc) or 50% NaI solution into the mesenteric artery, induced stronger and more widespread spasm, and then powerful rigidity of the abdominal muscles. (Fig. 13)

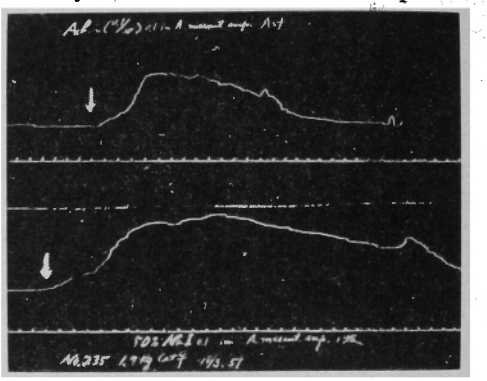


Fig. 13. Viceromotor reflex of decerebrate cat, upper ; ACH (0.1/50) 0.1cc lower ; 50% NaI 0.1cc injected into superior mesenteric artery.

4) The degree of contraction of the right and left abdominal muscles is almost the same. This indicates that all the alimentary canal is innervated bilaterally.

5) Faradization of the middle portion of the diaphragm did not cause the reflex phenomenon, but faradization of the peripheral portion of the diaphragm and parietal peritoneum caused powerful abdominal rigidity. This fact is clear from the innervation of the nerves of the diaphragm.

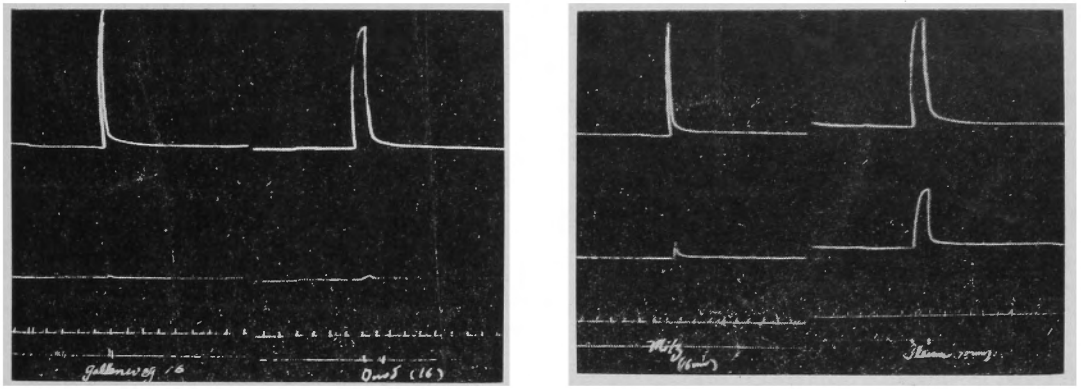
6) When the abdominal muscles are horizontally divided at the level of the 12 intercostal nerve, the proximal section of the muscle is innervated mainly by the intercostal nerves, from the 7th or 8th to 12th, and the caudal lobe, from 13th to the 3rd lumber nerve.

When the stomach, duodenum, biliary tracts or splenic artery was stimulated by faradization in this animal, the proximal section of the rectus muscles contracted, but not the distal lobe.

Of course the result was influenced by the intensity of the stimulus. If the stimulus was strong, the distal portion also contracted. Therefore I used threshold stimulus.

When the jejunum, ileum and appendix were stimulated, both muscle sections

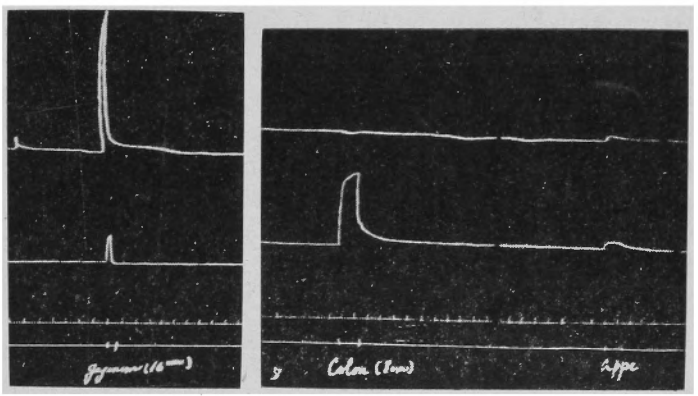
Fig. 14. Visceromotor reflex of decerebate cat by electric stimulation.
Upper ; cranial portion of rectus muscle. Lower ; caudal portion of rectus muscle.



Biliary way Duodenum Spleen-hilum Ileum

contracted. When the colon was stimulated, the proximal section of the mucsle did not contract, but the distal section showed reflex contraction. (Fig 14)

The rectus muscles were divided at various heights and by stimulating the viscera, contraction of both section of the muscles was recorded on the kymogramm.



Jejunum Colon Appendix

When the stomach was stimulated, the rectus muscle innervated from the 8th to 12th intercostal nerves contracted. The rectus muscle section contracts when the visceral afferent nerves are stimulated, which run into the spinal cord of the same heigh as the motor roots of the rectus muscles.

Stimulation of the duodenum :	Contraction of the rectus muscles innervated by the nerves T8-T12.
Jejunum :	T8-L1.
Biliary tracts :	T8-T12 or 13.
Spleen :	T8-L1.
Appendix :	T8-12.
Colon :	T13-L3.

These results are in accordance with the clinical observation of KIMURA and OHBA.

7) The reflex contraction of the abdominal muscles occurred after section of the splanchnic nerves. But it did not occur after splanchnectomy and lumbar sympathectomy. After exstirpation of the coeliac ganglion and superior mesenteric ganglion, stimulation of the stomach and the small intestine did not cause reflex contraction of the abdominal muscles, but stimulation of the colon did.

After exstirpation of the inferior mesenteric ganglion or lumbar sympathectomy, stimulation of the colon did not cause reflex contraction, but stimulation of the stomach, the small intestine and the appendix did.

These results show that the afferent pathways of visceromotor reflex arc from the small intestine pass mainly through the coeliac ganglion. Afferent pathways from the colon pass through the inferior mesenteric ganglion.

8) The facts above stated are supported by my experiments of posterior rhizotomy :

Stomach ; T5-T10 : Jejunum ; T5-T13 : Spleen and biliary tracts ; T5-T13 : Appendix and colon ; T12-L6.

These results are somewhat different from the results above mentioned. The reason is that in former experiments, I supposed, that rectus muscles were innervated by intercostal nerves below T7. After section of the splanchnic nerves, gangl on solare and 2nd lumbar sympathetic nerves, I still found visceromotor reflex by stimulation of the stomach, duodenum, and jejunum, but not by stimulation of the ileum, appendix and colon.

After section of the inferior mesenteric plexus and lumbar sympathetics, I did not find visceromotor reflex by stimulation of the colon, but I found it by stimulation of the alimentary canal above the ileum,

When the splanchnic nerves, 2nd to 6th lumbar sympathetics and ganglion solare were resected, visceromotor reflex caused by stimulation of the alimentary tract did not appear.

9) SMITHWICK found that after unilateral sympathectomy, visceral pain caused by distension of the intestinal tract by a balloon, or of the biliary tracts by water, was refered to the contralateral side. Following bilateral sympathectomy, pain caused by distension was abolished.

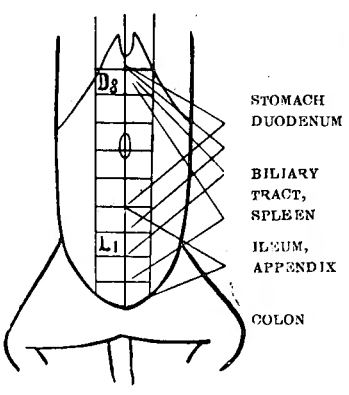


Fig. 15. Area of contraction of rectus muscle following visceral stimulation (with threshold stimulus.)

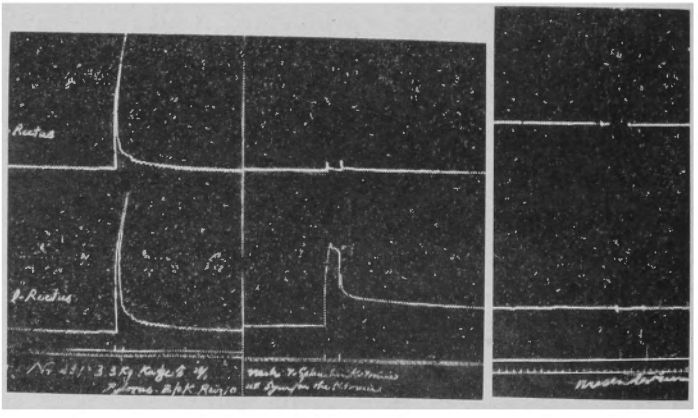


Fig. 16. male cat 3.3kg. Visceromotor reflex (upper curve; right rectus muscle, lower curve ; left muscle.) following stimulation of pylorus area before sympathectomy, after right side sympathectomy and both side sympathectomy. Note the decrease of visceromotor reflex of homolateral side after onesided sympathectomy.

The two kymogramms, in which the movement of both rectus muscles by stimulation of a viscus was recorded, showed almost the same curve. (Fig. 15.) After unilateral sympathectomy and transperitoneal lumbar sympathectomy, the reflex movement of the rectus muscle of the same side diminished or was almost abolished by stimulation of a viscus, but the other side contracted as before.

Following bilateral sympathectomy and splanchnectomy, contraction of each rectus muscle was abolished. (Fig. 16)

When visceral afferents are blocked unilaterally, the reaction of the rectus muscles of the same side becomes smaller. Therefore, concerning the afferents in sympathetic nerves, we can assume that the visceromotor reflex arcs are mostly homolateral, but a few are contralateral. These results are in correspondence with those of SMITHWICK.

10) Following section of the phrenic nerve or the vagus with the upper thoracic spinal cord, reflex contraction of abdominal muscles occurred. This fact shows that the vagus and phrenics do not play a roll in this reflex.

11) After section of the 8th, 9th and 10th dorsal roots of the thoracic spinal nerves, reflex movement of the abdominal muscles was demonstrated by stimulation of the stomach.

But it did not occur after section of the posterior roots T5-T13 on stimulation of the stomach, spleen and biliary tracts and after section of T12-L4 on stimulation of the colon.

MACSWINEY and SUFFORK studied the pupillo-dilator reflex as a pain reaction on cats and observed segmentary, bilateral and overlapped distribution of the afferent neurons from the stomach and small intestines.

My results are generally in agreement with his observations.

12) After injection of 10% TEAB 0.1-1.0cc, the impulses of the autonomic nerves were blocked, but the reflex contraction of rectus muscles was scarcely influenced.

13) After subarachnoid injection of absolute alcohol 0,2-0,5cc, this reflex movement became smaller than before. A small amount of JANUS-GREEN, NEUTRAL-RED injected with alcohol showed diffusion of alcohol from T10 to L3. Following spinal anesthersia with percamin-S, this reflex was abolished.

8. SOME CLINICAL OBSERVATION. (1)

From my experiments, I consider that the contralateralisation of visceral sensation by Ray and Neil after unilateral sympathectomy is not only a phenomenon in viscera, but also a phenomenon of the surface of the body.

I studied the ability to localize the points (local sign) in the midline of the abdominal wall in human beings after laparotomy with pararectus incision. Touching various points on the abdominal wall, I asked patients, who had an incision on one side, to tell which points were on the midline. Non operated patients felt the middle points of the abdominal wall almost correctly with differences of 0.5-1.0cm.

But most patients who had had laparotomy by right pararectus incision localised to the left when I touched the midline.

In extreme cases, the pararectus wound was felt on the midline of the abdominal wall. Lateral to the wound the skin was hyperesthetic and medial to it hypesthetic. The ability to localize of operated patients with pararectus incisions became vague and the points percieved by them as in the midline spread widely and were nearer to the wound than before operation. The length of the wounds which influenced localization was 5-20cm.

Fig. 17 shows the points percieved as in the midline by patients who had laparotomy with right pararectus incisions. Among 24 cases, patients who had lateralisation of the midpoints to the contralateral side were 19 cases: Not changed ; 4 cases : Laterlisation to non incised side ; 1 case.

But 2 points discrimination near the wound did not always change with contralateralisation of the local sign (SERA). From this point of view, the consciousness of the local sign generally depends not only on the discriminative ability of a sensory nerve but also on the integration of sensation transmitted by two or more afferents. The RAY and NEIL'S contralateralisation is attributed to the dysfunction of this integration. The integration of the sensory impulses serve as the judgement of the site of the starting point rather than the relative situation of two or more points. Therfore we call it the "initial local sign." Thus our experiments have made clearer the significance of the RAY-NEIL'S phenomenon. (Fig. 17)

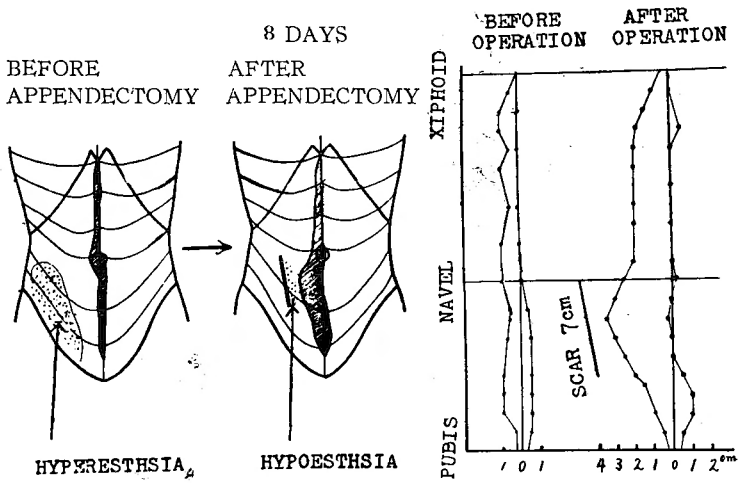


Fig. 17. A female, aged 17, feels a point, which is stimulated by light touche, for instance penciltip, within the shadowed area, as a point on the median line of the abdomen. After appendectomy the area has spreaded near the scar and yet a point on the true median line under the navel is felt by her as a point of the left side.

Some scholars said that so-called visceral pain did not occur in the viscus itself, but in the abdominal wall by the reflex contraction of the muscles. So contralateralisation of visceral sensation may be considered as alresult of viscerosomatic reflex on the abdominal wall. As stated above, unilateralsympathectomy caused visceromotorreflex to the abdominal muscles only on the contralateral side. Therefore my experiment seems to be in accordance with RAY-NEIL'S phenomenon.

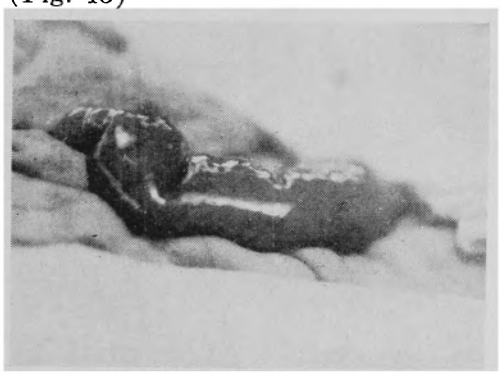
However visceral pain is not only referred pain, but there is also true viscerl pain. So this experiment is not enough to prove contralateralisation of visceral

sensation. The significance of contralateralisation will be well understood as a dysfunction of the initial local sign.

9. SOME CLINICAL OBSERVATION. (2)

Moore and others described that injection of some irritating chemicals into arteries of animals caused pain of blood vessels.

Injection of 50% NaI solution into the superior mesenteric artery caused cardialgia in 8 cases, injection of this chemical into the ileocolic artery caused cardialgia in 2 cases, but injection into epiploic artery did not cause pain in 3 cases. (Fig. 18)



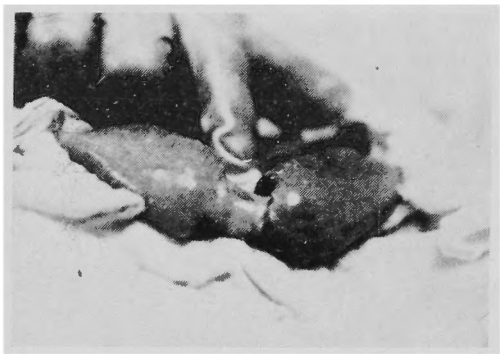


Fig. 18. Before injection of 50% NaI solution into a branch of the superior mesenteric artery. After injection.

Stretching or spastic contraction of the smooth muscle has been considered as an important mechanism causing visceral pain. I injected ACH (0.1gm/100cc) 0.1-0.2cc into a branch of superior mesenteric artery in 10 cases during laparotomy, pain was induced with spasm of the intestine.

When pain was caused, the intestine always showed spasm. Therefore I can assume that 50% NaI or ACH solution will work on the smooth muscle, and then contraction of the smooth muscles will act on sensory nerve endings. H. SETO, A. OTSU, demonstrated sensory nerve endings in various parts of the alimentary canal.

10. SOME CLINICAL OBSERVATIONS. (3)

1) The patients in whom appendices were stimulated by ACH (36 cases) or mesoappendices were ligated (95 cases) felt pain in the site close to the midline of the abdominal surface innervated by the nerves T5-T10, especially T8-T9. (Fig. 19)

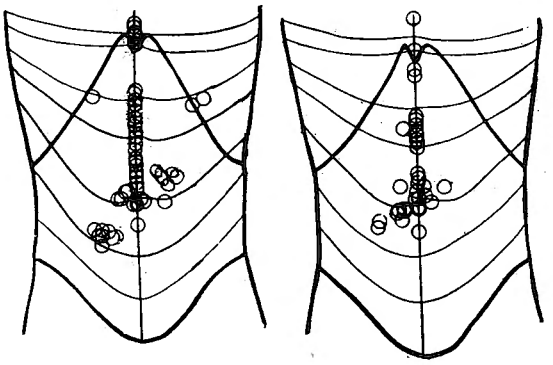


Fig. 19. The site of feeling of abdominal pain at the ligature of mesoappendix. Its localization is clear and its degree is strong. The site of referred pain from appendix by ACH method.

The relationship between the spread of spinal anesthesia and occurence of abdominal pain by ligature of mesoappendices (133 cases) and by stimulating appendices with ACH (87 cases) is shown in table 7.

When the level of complete anesthesia spreads over the dermatoma of T4 or T5, the abdominal wall relaxed and defensive muscular contraction was abolished completely, and all the patients did not feel pain on stimulation of the appendix.

2) Nausea and vomiting follwing the appendix under spinal anesthesia occured as shown in table 8. The relationship between the level of anesthesia and occurence of nausea and vomiting is not so clear. The reason is that the spinal

Table 7. Abdominal Pain following Stimulaion of Appendix or Mesoappendix under Spinal Anesthesia. in Clinical Cases.

Level of Anesthesia	Stimulus	Pain Positive	Uncomfortable feeling	No pain	Total
Over Th 4	a. Ligature of Mesoappendix		1	7	8
	b. VAG-ACH in the wall of appendix			3	3
Th 5	a.		2	7	9
	b.			6	6
Th 6	a.	5	3	4	12
	b.	2	1	4	7
Th 7	a.	9	3	1	13
	b.	3	3	3	9
Th 8	a.	13	3	5	21
	b.	8		5	13
Th 9	a.	25	4	2	31
	b.	14	1	11	26
Th 10 or under	a.	33	3	3	39
	b.	9	2	12	23
Total	a.				133
	b.				87

Table 8. Nausea and Vomiting following Stimulation of Appendix or Mesoappendix in clinical cases.

Level of Anesthesia	Stimulus	Vomiting Positive	No vomiting	Total
Th 4 or over it	a. Traction or ligature of mesoappendix	2 (25 %)	6	8
	b. VAG-ACH in appendix		3	3
Th 5	a.		9	9
	b.	4 (66.6%)	2	6
Th 6	a.	4 (33.3%)	8	12
	b.	4 (44.3%)	3	7
Th 7	a.	4 (30.7%)	9	13
	b.	4 (33.3%)	6	9
Th 8	a.	12 (60 %)	8	20
	b.	6 (58 %)	6	12
Th 9	a.	16 (58.2%)	11	27
	b.	10 (38.5%)	16	26
Th 10	a.	12 (38.9%)	19	31
	b.	8 (34.7%)	15	23
Local anesthesia	a.	2 (17 %)	10	12
	b.		12	12
Total	a.			132
	b.			88

anesthesia itself may cause nausea and vomiting, and that the vagal nerves are principal ways to conduct afferent emetic impulses.

3) The effects of injection of absolute alcohol into the subarachnoid space in 16 patients who had abdominal pain or other symptoms are shown in table 9.

Table. 9. Clinical Cases Receiving Subarachnoid Alcohol Injection.

No. of Cases Age and Sex	Site of Puncture	Amount of Alcohol	Symptoms	Effect
(1) 51 F			Lumbago accompanying carcinoma of rectum	Improved
(2) 49 M	Th 8–9	0.5 cc	Dumping syndrome after gastrectomy	Improved
(3) 54 F	Th 9–10	0.4 cc	Meteorism	Improved
(4) 69 M	Th 8–9	0.5 cc	Visceral pain caused by pancreatic carcinoma	A little improved
(5) 57 F	Th 9–10	1.0 cc	Lumbago accompanying carcinoma stomach	Improved
(6) 51 M	Th10-L3	2.5 cc	Abdominal pain and lumbago with stomach carcinoma	A little improved
(7) 50 M	Th 5–6	1.5 cc	Abdominal pain with stomach carcinoma	A little improved
(8) 33 F			Obstipation	Unchanged
(9) 38 F			Polakisuria	〃
(10) 20 F	Th 7–8 Th 8–9	0.3 cc 0.5 cc	Abdominal pain after appendectomy	〃 〃
(11) 24 M	Th 10-11	0.5 cc	Abdominal pain with intestinal tuberculosis	〃
(12) 26 M	Th 10-11 Th12-L1	1.0 cc 0.5 cc	〃	〃 〃
(13) 51 M	Th 8–9 Th 7–8	0.8 cc	Abdominal pain with stomach carcinoma	〃 〃
(14) 25 M	Th 10-11	1.0 cc	Abdominal pain after appendectomy	〃
(15) 46 M	Th 8–9	2.0 cc	Abdominal pain with stomachcarcinoma	〃
(16) 20 M	Th 10-11	1.0 cc	Abdominal pain with chronic appendicitis	〃

SUMMARY.

Visceral pain accompanies many reflex phenomena, especially in decerebrate animals (SHERRINGTON). To study visceral sensation, I employed various reflex criteria, such as changing of respiration, blood pressure, pupillo-dilator reflex, visceromotor and vomiting reflex.

The results such as increase of blood pressure, dilatation of pupils and so on, should be considered as the results of excitation of sympathetic system.

There may be changing of humoral substance in blood by visceral pain. I demonstrated it by MUSSER-GRIMM'S method. The blood tends to become adrenergic soon after vomiting or administration of great dosis of ACH. A humoral effect of some inhibitory substance can not be completely excluded in my study of the intestinal inhibitory reflex. However, since adrenalectomy did not reduce the degree of this reflex, I consider that the neurogenic reflex plays a greater roll than the humoral effect.

The afferent pathways which are responsible for anorexia and vomiting are in the vagi and only in some exceptional cases the splanchnic nerves.

The visceromotor reflex has the most simple reflex arc among these reflex phenomena. The reflex arc involves afferent fibers only in the splanchnic nerves. In this reflex, afferent fibers in the vagi, even if they exist, play a minor role.

The visceromotor reflex of decerebrate cats was utilized to determine the distribution of afferent fibers of the splanchnic nerves to the spinal roots through which they enter the spinal cord. Wide segmental overlapping innervation of afferent nerves was established as in efferent nerves. And yet afferent nerve fibers from a viscus may spread widely in the sympathetic trunk and enter the spinal cord at several levels, from which efferent nerves run to the rectus muscles of both sides.

Experiments of unilateral sympathectomy show that a few afferent fibers may cross to the other side. And there is a relationship between the lateralisation of the visceromotor reflex and contralateralisation of visceral pain (SMITHWICK et al) as well as between these and initial local sign (KIMURA).

My experiments of spinal anesthesia and injection of alcohol into the subarachnoid space, show that the vagi probably do not conduct impulses from the abdominal viscera except emetic impulses.

I am much indebted to Assist. Prof. Ch. KIMURA, M. D. of our clinic for his constant help throughout my study. And this was read by him as a part of his thema "Operation of Autonomic Nervous System" at the 51 : Annual Meeting of the Japanese Surgical Association. on April 1～3.1951, Tokyo.

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内臓性反射に関する研究

京都大学医学部外科学第2講座（青柳安誠教授 指導）
渡　辺　　裕

1. 内臓痛の場合種々の反射性随伴現象が現われる．内臓痛の適刺戟としてアセチルコリン（Ach）注射法，電気刺戟，機械的刺戟を用い，動物では呼吸運動，瞳孔散大反射，胃腸運動抑制反射，内臓運動反射，血圧反応，嘔吐の随伴現象を指標として脊髄以下末梢の内臓知覚路を検討した．

2. 呼吸運動，瞳孔散大反射を指標とした場合，主に廻腸からの求心路は①内臓神経，脊髄後根，脊髄，②交感神経節状索，交通枝，③迷走神経であつた．

3. 去脳猫，無麻酔猫の嘔吐の主求心路は迷走神経で，交感神経も之に与り，嘔吐は腹膜症状と解するよりも内臓性又は迷走神経症状と云うのが適当である．又嘔吐直後の血中自律神経作用物質はむしろ adrenergic である．

4. Ach液の腸管壁滴下及び注射時，腸間膜動脈内注射時血圧上昇を来し，筋肉内及び静脈内注射時には血圧下降を来し，前者は交感神経性反応であり且つ人体では内臓痛として感ずる．

5. TEABに依り侵害反射は血圧以外，影響を受けない．臨床的に内臓痛の寛解する事の多いのは，一部腸管運動の抑制作用に依るが，TEABは，腸管運動に対し両働性に作用し，促進的と認められる状態の時に抑制作用を呈する．即ち自律神経緊張度の高い方を抑制する．

6. 内臓運動反射は最も簡単な反射弓を形成し，去脳猫の内臓を刺戟時，両側直腹筋は略々同程度に収縮し，且つ閾刺戟時には各消化管部位に応じて断区的に反応し，後根切断実験の結果と類似して居る．

一側交感神経切除後同側の直腹筋収縮は低下し反対側は元通りであり，両側切除時内臓運動反射は消失した．即ち交感神経に関して求心性支配は大部分同側性，一部交叉性である．之は人体に於いて1側胸腰部交感神経切除後の内臓痛反対側移動と一致する．又人体の腹壁の正中線附近は左右重複性に求心性支配を受け腹部皮膚上の一点の部位感覚（右か真中か左か）が生ずるが，1側で開腹術をうけ神経の切断された場合，術後は皮膚上の部位感覚は対側に移動する．即ち基準になる部位感覚の移動が起る．以上三者の間には基本的な類似が存する．

7. 人体虫垂のAch刺戟時内臓痛放散部は，Th_{5-10} 殊に Th_{8-9} のデルマトームの部であり，又，虫垂の痛みには関連痛の他に真の内臓痛も存する様である．

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